

# Variable Selection Results

Nirupama Tamvada

## Simulation Settings: Simulating from Cause-Specific Cox Proportional Hazards Model

- We generate data from two cause-specific Weibull hazards according to Beyersmann et al. 2009
- The survival times for both causes are generated according to the following formula:

$$T = \left( -\frac{\log(U)\lambda}{\exp(\beta X)} \right)^{1/v}$$

- Cause 1 is generated from a Weibull hazard with baseline hazard ( $\lambda$ ) 0.55 (when all the covariates are set to 0) and the shape parameter ( $v$ ) set to 1.5. Cause 2 is also generated from a Weibull hazard of baseline hazard 0.35, with the shape parameter also set to 1.5.
- The cause-specific indicator is generated from a binomial experiment with  $p = \frac{\alpha_{01}}{\alpha_{01} + \alpha_{02}}$  (i.e the denominator represents the all-cause hazard)
- Any survival times less than 1/365 or greater than 1 were winsorized, i.e converted to be within a 1.5 year range (with white noise added so as to not have too many recurrent values)
- The  $X$  covariates are generated from a multi-variate normal distribution with  $\mu = 0$  and a block correlation setting with 4 blocks with correlations 0.7, 0.4, 0.6, and 0.5. The noise covariates were generated with pairwise correlations 0.1.
- The censoring times are generated by an exponential distribution changed so that we have two censoring settings: 30 % censoring and 50% censoring

## Models under comparison

- Cause-specific Independent Cox Model (with Elastic Net  $\alpha = 0.7$ ) (enet-iCox)
- Cause-specific Cox with common penalty (with Elastic Net  $\alpha = 0.7$ ) (enet-penCRCox)
- Casebase (with Elastic Net  $\alpha = 0.7$ ) (enet-Casebase)
- Tapak et. al (2015) found elastic-net better than LASSO in a block-correlation setting

## Simulation Parameters

1.  $N = 400$
2.  $p = 120, p = 1000$
3. Number of true covariates ( $Tp = 20$ )
4. Censoring: 30 % (leads to  $\sim 47\%$  cause of interest) and 50% (leads to  $\sim 30\%$  cause of interest)
5. Cause 2 > Cause 1

## Simulation Settings

1.  $N = 400, p = 120$ , Varying effects between  $\beta_1$  and  $\beta_2$  censoring: 30 % , Cause 1 > Cause 2. This mimics biological biomarker data with varying block effects on both causes.
2.  $N = 400, p = 120$ , Varying effects between  $\beta_1$  and  $\beta_2$  censoring: 50 % , Cause 1 > Cause 2. This mimics biological biomarker data with varying block effects on both causes.
3.  $N = 400, p = 120$ , Varying effects between  $\beta_1$  and  $\beta_2$  censoring: 30 % , Cause 2 > Cause 1. This mimics biological biomarker data with varying block effects on both causes. Cause 2 is often greater in Cause 1 in sparse datasets where the risk curves cross.
4.  $N = 400, p = 1000$ , Varying effects between  $\beta_1$  and  $\beta_2$  censoring: 30 % , Cause 1 > Cause 2. This mimics biological biomarker data with varying block effects on both causes.
5.  $N = 400, p = 1000$ , Varying effects between  $\beta_1$  and  $\beta_2$  censoring: 50 % , Cause 1 > Cause 2. This mimics biological biomarker data with varying block effects on both causes.
6.  $N = 400, p = 1000$ , Varying effects between  $\beta_1$  and  $\beta_2$  censoring: 30 % , Cause 2 > Cause 1. This mimics biological biomarker data with varying block effects on both causes. Cause 2 is often greater in Cause 1 in sparse datasets where the risk curves cross.

7.  $N = 400$ ,  $p = 120$ , effects only on cause 1 ( $\beta_2 = 0$ ) censoring: 30 % , Cause 1 > Cause 2. This mimics the scenario where Cause 2 is death so there may not be any covariates associated with this.
8.  $N = 400$ ,  $p = 120$ , opposite block effects of  $\beta_1$  and  $\beta_2$  censoring: 30 % , Cause 1 > Cause 2. This mimics the scenario of different biological pathways related to two relevant biological endpoints.
9.  $N = 400$ ,  $p = 120$ ,  $\beta_1 = -\beta_2$  censoring: 30 % , Cause 1 > Cause 2. This scenario might resemble cancer therapy, i.e when patients are treated with chemo which may be associated with higher non-cause 1 mortality.
10.  $N = 400$ ,  $p = 1000$ , effects only on cause 1 ( $\beta_2 = 0$ ) censoring: 30 % , Cause 1 > Cause 2. This mimics the scenario where Cause 2 is death so there may not be any covariates associated with this.
11.  $N = 400$ ,  $p = 1000$ , opposite block effects of  $\beta_1$  and  $\beta_2$  censoring: 30 % , Cause 1 > Cause 2. This mimics the scenario of different biological pathways related to two relevant biological endpoints.
12.  $N = 400$ ,  $p = 1000$ ,  $\beta_1 = -\beta_2$  censoring: 30 % , Cause 1 > Cause 2. This scenario might resemble cancer therapy, i.e when patients are treated with chemo which may be associated with higher non-cause 1 mortality.

### **Simulation Settings: Misspecified Model (Proportional sub-distribution hazards = non-proportional cause-specific hazards)**

- We generate data based on a two-cause model specification according to Fine and Gray (1999).
- Any survival times less than  $1/365$  or greater than 1 were winsorized, i.e converted to be within a one-year range (with white noise added so as to not have too many recurrent values)
- The causes were generated through a binomial experiment with  $p = (1 - p_0^{e^{x\beta_1}})$  with  $p_0$  set to 0.6 to generate Cause 1 as the cause with the largest incidence
- The censoring times are generated by a uniform distribution  $U[0, M]$  with  $M$  changed so that we have two censoring settings: 30 % censoring and 50% censoring
- The  $X$  covariates are generated from a multi-variate normal distribution with  $\mu = 0$  and a block correlation setting with 4 blocks with correlations 0.7, 0.4, 0.6, and 0.5. The noise covariates were generated with pairwise correlations 0.1.

### **Models under comparison**

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- Casebase (with Elastic Net  $\alpha = 0.7$ ) (enet-Casebase)

### **Simulation Parameters**

1.  $N = 400$
2.  $p = 120, p = 1000$
3. Number of true covariates ( $Tp = 20$ )
4. Censoring: 30 % (leads to  $\sim 47\%$  cause of interest)

### **Simulation Settings**

13.  $N = 400, p = 120$ , Varying effects between  $\beta_1 = -\beta_2$  censoring: 30 %
14.  $N = 400, p = 1000$ , Varying effects between  $\beta_1 = -\beta_2$  censoring: 30 %